Case Report

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Primary ciliary dyskinesia: two different clinical cases

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ABSTRACT

Primary ciliary dyskinesia (PCD) is a clinically and genetically heterogeneous condition characterized by defective motile cilia activity. It is a rare disease with a frequency of 1 in 15.000-20.000 people and is generally inherited in an autosomal recessive and X-linked disease pattern. The diagnosis of PCD becomes easier when the patient has situs inverus anomaly accompanying recurrent lower and upper respiratory tract infections, as in our second case. However, it becomes vice versa in the absence of a situs anomaly. In this case report, we present two PCD patients with diverse clinical characteristics, one with Kartagener's syndrome and the other without these features.

Keywords: Primary ciliary dyskinesia, Kartegener syndrome, recurrent lung infections

INTRODUCTION

Primary ciliary dyskinesia (PCD) is a clinically and genetically heterogeneous condition characterized by defective motile cilia activity (1). It is a rare disease with a frequency of 1 in 15.000-20.000 people and is generally inherited in an autosomal recessive and X-linked disease pattern (2). PCD is characterized by reduced ciliary movement, immotility, or pattern change (ciliary dyskinesia). Asymmetry occurs since the nodal cilia regulating the normal position of the heart and internal organs are defective in the embryonic period (3). Kartagener's 1933 description of the illness, which included the three symptoms of sinusitis, bronchiectasis, and situs inversus. After this definition Afzelius reported in 1976 that the pathogenesis is connected to a defect in the cilia's structure or function. The subsequent research in the following years preferred the term "ciliary dyskinesia" instead of "ciliary immotility" since it was documented that the disease develops even in the presence of motile cilia (4,5).

In this case report, we present two PCD patients with diverse clinical characteristics, one with Kartagener's syndrome (sinusitis, bronchiectasis, and situs inversus) and the other without these features. We emphasized that a patient without situs inverus but with a recurrent lung infection and bronchiectasis may also have a diagnosis of PCD.

CASE

First Case

A 17-year-old female patient was referred to our pediatric pulmonology clinic due to chronic wet cough and recurrent lung infections. The patient had chronic respiratory distress since five years old and a history of hospitalizations brought on by recurrent bronchiolitis. Inhaled steroid treatment had also been administered to the patient due to the intermittent shortness of breath accompanying the cough complaint, but the patient's complaints did not improve. We also learned she had a wet cough throughout the year, particularly in the winter months. Besides, her condition improved when using antibiotics, but the cough with sputum showed up again afterward. The patient also had concomitant nasal congestion and purulent nasal discharge and was treated for recurrent sinusitis. She was delivered vaginally at the expected time and spent about two weeks in the hospital's intensive care unit as a result of respiratory distress. She had no previous infection history other than upper and lower respiratory tract infections. No other known illness affected her. We identified consanguinity between the parents in the family history. Three of her siblings were in good health.

The left lung was found to have atelectasis on the patient's chest X-ray (**Figure 1a**), while the right lung had expanded to the left. Firstly, we performed

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an etiology-oriented bronchoscopy on the patient because of the atelectatic area in the lungs. The findings revealed that the lingula of the left lower lobe was occluded with purulent sputum, and it was aspirated and cleared. Yet, we did not observe no foreign body or airway malformation was observed. The patient was given intravenous antibiotic therapy for the lung infection. Then, the thorax tomography demonstrated tree-in-bud patterns (**Figure 1c**) and bronchiectasis (**Figure 1d**) changes in the lingula of the left lung. Moreover, there was H. influenza growth in the patient's bronchoalveolar lavage sample. acid-fast bacilli and tuberculosis polymerase chain reaction results were negative.

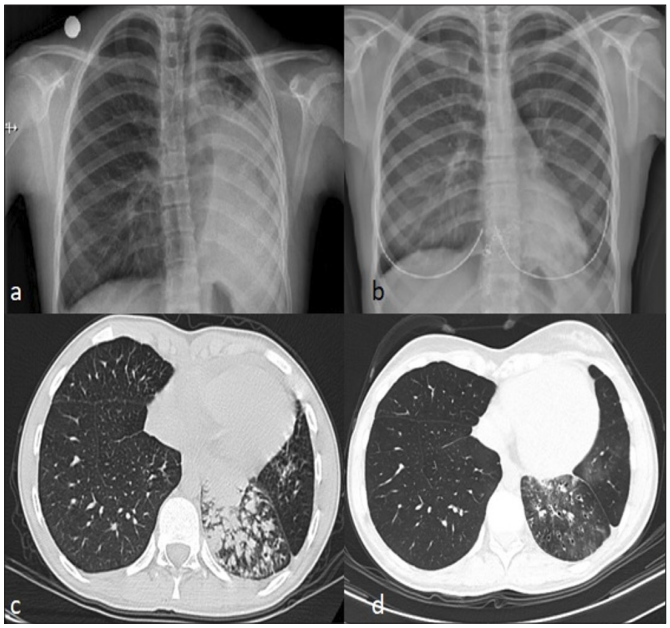

Figure 1: 1a: Atelectasis while the right lung was expanded to the left, **1b:** after bronchoscopy and antibiotic therapy, **1c:** tree-in-bud patterns, **1d:** bronchiectasis

In the screening for immunodeficiency for revealing the other possible bronchiectasis, the patient did not have lymphopenia or neutropenia. In addition, immunoglobulin A, immunoglobulin G, and immunoglobulin M levels were found to be within the reference ranges by her age. Lymphocyte subgroups were within normal limits by her age. Vaccine (hepatitis, measles, rubella) responses of the patient were also within normal age-appropriate limits. While tuberculin skin size was 5 mm, the chlorine level in the sweat test was 13 mmol/L.

The patient who had respiratory distress during the newborn period, recurrent sinusitis, and a current lung infection was found to have a pathological mutation in the CCD40 gene as a result of the whole exon sequencing (WES) analysis that was sent for PCD. As a result, PCD was identified in the patient.

Second Case

A 15-year-old male patient with a persistent cough, sputum production, and dextrocardia was referred to our pediatric pulmonary clinic. We discovered that the patient was hospitalized in the intensive care unit due to respiratory distress in the newborn period and then hospitalized a couple of times due to recurrent lung infections. Moreover, he had recurrent sinusitis, an ear tube due to recurrent otitis, and partial hearing loss in the right ear. He did not have any other known disease in his medical history. In the family history, the patients and the other two siblings were all healthy. The parents were related by the third degree of consanguinity.

There were pericardial infiltrates on the left and behind the heart on the right of the chest X-ray, and the heart and stomach fundic gas shadows were on the right. (Figure 2a). He had bronchiectasis (Figures 2b, 2c), and tree-in-bud patterns (Figures 2d) on thorax tomography. We first considered Kartegener's syndrome in the patient with the triad of recurrent sinusitis, bronchiectasis, and situs inversus totalis. WES analysis resulted in DNAAF2 homozygous pathogenic mutation; thus, the patient was diagnosed with PCD.

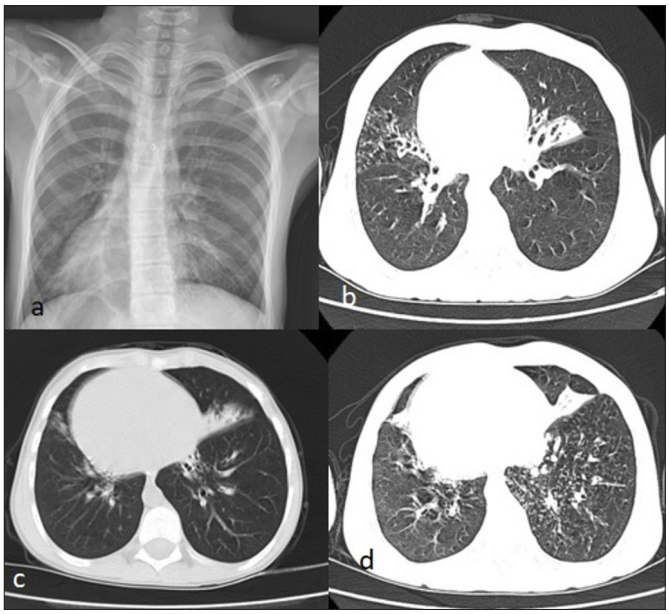

Figure 2: 2a: Situs inversus totalis, **2b:** bronchiectasis, **2c:** bronchiectasis, **2d:** tree-in-bud patterns

DISCUSSION

PCD is a condition emerging due to impaired cilia structure or function in the epithelial cell in the respiratory tract. Disrupted cilia structure causes the secretions in the airway not to be removed from the lungs, that is, impaired mucociliary clearance, which will eventually lead to inflammation in the upper and lower respiratory tract and recurrent respiratory tract infections (6). Possible causes, such as immunodeficiency,

cystic fibrosis, lower respiratory tract malformations, and foreign body aspiration, should be excluded in patients with recurrent respiratory tract infections. The diagnosis of PCD becomes easier when the patient has situs inverus anomaly accompanying recurrent lower and upper respiratory tract infections, as in our second case. However, it becomes vice versa in the absence of a situs anomaly, as in our first case; thus, there needs to make a differential diagnosis with other recurrent lower respiratory tract conditions.

Diagnosing PCD may not be easy in contemporary conditions. The European Respiratory Society (ERS) and the American Thoracic Society (ATS) have published two evidence-based guidelines for the diagnosis of PCD (7,8). However, there is still no gold standard diagnostic test for PCD. Both guidelines recommend the use of a combination of tests, including nasal nitric oxide measurement, high-speed video microscopy analysis, immunofluorescence analysis, transmission electron microscopy analysis, and genotype analysis (7, 8). Due to the physical setup of our clinic, we were unable to use all of these tests. Therefore, we confirmed the diagnosis upon the results of genetic analyses for our patients. It should not be forgotten that genetic analysis has made it possible to diagnose only 70% of patients today. (9); thus, patients with high clinical suspicion may need to be referred to advanced clinical centers, and their diagnosis should be confirmed with the results of other tests.

Various risk markers were previously established to determine which patients should be diagnosed with PCD and for further investigation. In this regard, the ATS defined four markers in 2016: the presence of laterality defect, unexplained respiratory distress lasting longer than 24 hours in term newborns, early-onset persistent nasal congestion, and early-onset productive cough. The specificity becomes above 96% upon the presence of at least three of these clinical markers, while it becomes above 98% upon the presence of all these markers (10). In addition, another study introduced a scoring tool called Primary Ciliary Dyskinesia Rule (PICADAR) (11). In this scoring system, patients are scored according to their symptoms, and there are seven markers in addition to persistent productive cough: term delivery, neonatal chest symptoms, history of neonatal intensive care unit admission, chronic rhinitis, ear symptoms, situs inversus, and a congenital heart defect. The PICADAR score is a guide for deciding further evaluation of diagnostic testing in PCD. A PICADAR score of 10 or higher indicates the probability of PCD to be over 90%, while patients should be evaluated for PCD in the case of a PICADAR score of 5 or higher (11). Hence, utilizing these two different PCD evaluation criteria would grant an idea about whether further examination is requested in the case of a patient presenting with chronic cough.

CONCLUSION

PCD is among the rare diseases in children. It may be consider PCD in patients with a chronic productive cough and situs anomaly. However, PCD may also be kept in the pocket as a differential diagnosis in patients with a productive cough and recurrent lower respiratory tract infections without situs anomalies.

ETHICAL DECLARATIONS

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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